ARGUMENTS/REMARKS

Claims 1 and 31-75 are in the application.

No claims are amended herein.

Entry of this Reply, reexamination and reconsideration of the application are respectfully requested in light of the following remarks.

Rejection Under 35 USC §112, First Paragraph

Claims 1 and 31-75 stand rejected as lacking enabling disclosure. Applicants respectfully traverse this rejection for at least the following reasons.

Applicants maintain the objection to the timing of this rejection.

Despite the untimely nature of this rejection, Applicants respond as follows.

Applicants note that U.S. Patent No. 7,129,080, which is commonly owned with the present application, discloses and claims IFDO as a model for prions, for the purpose of avoiding the pitfalls involved with the use of actual prions. Such known problems include contamination, incomplete sterilization possibly leading to unknown infection of humans or test animals and problems relating to certainty of removal of prions after testing. As disclosed from col. 2, line 61 to col. 3, line 21 of US 7129080, due, e.g., to the unavailability of priocidal treatments, the resulting concerns among medical personnel, the difficulty in identifying a prion infection until it is too late, there remained a need for an improved method of evaluating priocidal activity. That improved method, in one embodiment of US 7129080, involves the use of IFDO. Based on the disclosure of US 7129080 alone, Applicants respectfully submit that the presently claimed invention was fully enabled to the person of skill in the art in accordance with 35 U.S.C. 112, 1st paragraph, at the time the present application was filed.

Furthermore, Applicants note that U.S. Patent No. 7,001,873, also commonly owned with the present application, claims a method of deactivating prions and uses both IFDO and a BSA denatured protein as prion models. As disclosed at col. 5, lines 23-26, BSA adopts a high β-sheet conformation which is similar to infectious prior protein. The compositions disclosed in US 7001873 worked comparably against both the IFDO and the

BSA denatured protein prion models. The fact that US 7001873 used IFDO as a model for prions shows that the USPTO has previously accepted such data as a prion model.

Similarly, U.S. Patent Nos. 7,071,152, 7,129,080, 7,217,685, 7,393,818 and 7,803,315, all commonly owned with the present application, have been granted using IFDO as a model for prions. Quite clearly, both the USPTO and those of skill in the art have recognized the efficacy and enablement of the IFDO model for prions.

The foregoing directly rebuts the Examiner's arguments regarding enablement.

Applicants respectfully submit that the present claims are fully supported by enabling disclosure in the specification. Based on the disclosure of the foregoing U.S. patents, Applicants respectfully submit that the presently claimed invention was fully enabled to the person of skill in the art in accordance with 35 U.S.C. 112, 1st paragraph, at the time the present application was filed.

Applicants submit herewith another publication, which further substantiates the use of IFDO as a valid, art-recognized model for investigating TSE agents such as prions. The publication is Burdon, D.W., et al., "Replication of IFDO on a chemically defined medium," *J. Med. Microbiol.*, Vol. 45, pp 10-15 (1996) ("Burdon, 1996"). A copy of this publication is submitted together with the present Reply.

As stated in the Abstract of Burdon, 1996, the findings reported "are consistent with the hypothesis that IFDO is a replicating agent that utilizes specific preformed protein to assemble a proteinaceous particle, and support the postulated relationship of IFDO to transmissible spongiform encephalopathy agents ." The conclusion of the publication is reproduced here:

> In conclusion, the data presented are consistent with IFDO being a primitive biological agent with a nucleic acid which does not encode for any other macromolecule, but which can recognise haemoglobin and utilise it to assemble a proteinaceous particle. These observations reinforce the hypothesis that IFDO is a TSE-like agent and that it provides a valid model for investigating the nature of TSE agents [l].

The foregoing directly rebuts the contention in the Office Action that the earlier Burden publication "is only in reference to the ability of IFDO to assemble as a proteinaceous protein, in contrast to a prion model for evaluating structural properties under certain chemical conditions." This further rebuts the Examiner's argument that since the claims are drawn to inactivating prions, while Applicants' examples employ IFDO to the claimed treatments, this supports the rejection.

In addition to the foregoing, Applicants submit herewith an abstract of another published paper disclosing IFDO as a model for the agent ("CJA") causing Creutzfeldt-Jacob disease, which is also thought to be a prion. The article is Dyas, A.C., et al., "Studies of a novel agent possessing resistance to moist heat and disinfectants: parallels with Creutzfeldt-Jacob agent," *J. Hosp. Infect.*, 15(3), April 1990, pp. 265-72. Applicants do not have readily available a copy of the complete article, but expect the Examiner to be able to obtain same, if necessary. The article states that the IFDO agent may provide a valid model for sterilization of items contaminated with CJA. This article provides further evidence that those of skill in the art were enabled, at the time the application was filed, to make and use the presently disclosed and claimed invention in accordance with 35 U.S.C. 112, 1st para.

As shown by both Burden articles, the person of skill in the art would have been fully enabled to make and use the present invention against both actual prions and an IFDO model, at the time the present application was filed.

The Examiner has failed to state any factual basis for these contentions, merely contending, based on speculation, that IFDO is not a valid model for prions. As for the Examiner's attempted rebuttal of Applicants' point that IFDO would be used rather than actual prions for safety reasons, it is quite logical that any person of skill in the art would prefer to work with something likely to be less dangerous that a very unknown agent such as prions. This is in fact explicitly disclosed in the above-referenced US 7129080.

As for the Examiner's contention that establishing a correlation between an IFDO and a prion taking "much undue experimentation", such establishing is in fact exactly what Applicants have done in the present application and in the above-identified commonly-

owned U.S. patents. Applicants have enabled the use of the claimed agents with IFDO, and all that remains is for this to be applied to actual prions. This is not undue experimentation, this is simply carrying out Applicants' disclosed and claimed invention in accordance with the knowledge of the skilled person.

Applicants respectfully submit that, in light of the two Burden articles, the Dyas abstract and the above-identified, commonly-owned U.S. patents, that Applicants' disclosure fully enables the skilled person to make and use the claimed invention. Based on the foregoing, Applicants respectfully submit that the presently claimed invention is fully enabled to the person of skill in the art in accordance with 35 U.S.C. 112, 1st paragraph.

For all of the foregoing reasons, Applicants respectfully submit that the presently claimed invention is, and was at the time the present application was filed, fully enabled in accordance with 35 USC §112, 1st paragraph, and accordingly Applicants respectfully request withdrawal of this ground of rejection.

Rejections Under 35 USC §103(a)

Claims 1, 31-40, 45-52 and 55-74 stand rejected under 35 U.S.C. §103(a) as unpatentable over Prusiner (US 6720355) and Ernst and Race (Ernst et al., "Comparative analysis of scrapie agent inactivation methods," *Journal of Virological Methods*, 41 (1993) 193-202). Claims 54 and 75 stand rejected as obvious over Prusiner and Ernst and Race, and further in view of Foster, (US 7252720). Claim 53 stands rejected as obvious over Prusiner and Ernst and Race, and further in view of McDonnell (US 7001873) and/or Narayanan (US 5326789).

Applicants respectfully traverse each of the foregoing rejections for at least the following reasons, as well as for the reasons set forth in the previous Reply to Office Action, which are incorporated herein by reference.

In response to Applicants' previous arguments, the Examiner again contended that these results are somehow undermined or are less legitimate since IFDO was used as the target or test material, as opposed to actual prions. Appellants respectfully submit that for the reasons set forth above, IFDO is in fact a suitable model for investigating agents for use

against prions, and that persons of skill in the art already know and accept this. Given that Applicants have shown quite unexpected results in the Examples using IFDO, and given that the foregoing patents and the two Burden publications fully support use of this model, Applicants again submit that the unexpectedly good results reported in the Examples fully rebut any possible *prima facie* case of obviousness.

To the extent that the obviousness rejections are based on the alleged lack of enablement, this alleged basis has been fully addressed and rendered moot by the foregoing.

Applicants respectfully submit that the obviousness rejections lack basis and should be withdrawn, since no *prima facie* case of obviousness has been stated.

Even if the Office Actions have set forth a *prima facie* case of obviousness, Applicants' examples show a synergistic effect that overcomes any such *prima facie* case. In each instance, superior results are obtained when the formulations within the scope of the Applicants' claims 1 and 56 are used, as compared to similar formulations outside the scope of the present claims.

Thus, even if it might have been *prima facie* obvious to combine the sulfonate of Prusiner with a composition such as the LpH formulation, Applicants' examples show that an unexpected synergy is exhibited by the claimed combination, which could not have been expected based on the disclosures of the prior art.

The results shown in Table 1, at page 15, compare formulations within the scope of the presently claimed invention against the LpH™ of Ernst and Race. In all cases, the presently claimed invention provides unexpectedly superior Log reduction of IFDO. It is noted in this regard that Log reduction is a logarithmic scale, so that the Log reduction of Composition I, reported at 5.1, is more than ten times better than the Log reduction of 4.0 reported for the LpH™ of Ernst and Race, which does not contain an alkyl or alkylbenzene sulfonate. The Log reduction of Composition VII, reported at 6.7, is several hundred times better than the Log reduction of 4.0 reported for the LpH™ of Ernst and Race. Thus, Applicants respectfully submit that a synergistic effect has been shown for the method using the composition of claim 1.

The results in Table 2, at pages 16-17, directly tests the Log reduction of IFDO obtained with compositions containing phenols other than those specifically recited in claims 1 and 56 together with an alkyl or alkylbenzene sulfonate, and in all cases, the test results using those compositions are inferior to the test results using compositions in accordance with the present invention. Here, again, a synergistic effect is shown by the presently claimed invention when compared to the method using very similar compositions outside the scope of the present invention.

Therefore, Applicants respectfully submit that this evidence, in the application examples, fully rebuts any possible *prima facie* case of obviousness.

For the foregoing reasons, Applicants respectfully submit that the presently claimed invention of claims 1 and 56, and the claims dependent thereon, would not have been obvious over Prusiner in view of Ernst and Race.

Claim 45 would not have been obvious for an additional reason: the Office Action fails to state a legally correct *prima facie* case of obviousness, since the rejection is supported by nothing more than speculation about what might have happened.

Claim 45 recites that at least one of the phenols in the combination of phenols has a Log P_c value of at least about 2.5. As noted in the specification at page 13, lines 29-37, Applicants found that the solubility of the phenol in the composition has an effect on the degree to which the protein is complexed, and that, in general, the lower the solubility of the phenol in the formulation, the greater the degree of complexation, i.e., the more effective the phenol formulation is at prion inactivation. Example 3 correlates the partition coefficients, expressed as log P_c, with the results in log IFDO reduction.

Despite its lack of citation to any authority, the Office Action, at page 9, contends that it would have been obvious to combine the teachings of Prusiner and Ernst and Race to include at least one phenol with a Log P_c value of at least about 2.5. As Applicants noted in the previously Reply to Office Action, this contention is completely unsupported by any citation to any authority or disclosure. There is simply no evidence that would have even suggested such a factor could possibly be important in selecting at least one phenol for

inclusion in a composition for use in a method of inactivating prions. Accordingly, there is no basis for this rejection and it should be withdrawn.

Applicants' argument relating to the use of water in Prusiner and Ernst and Race simply notes that, since these references teach aqueous media, that such teaching would, if anything, lead one away from the use of a phenol having a greater hydrophobicity, which is what Log P_c measures. Since the prior art uses an aqueous system, absent any teaching to the contrary, a person of ordinary skill would expect agents having greater hydrophilic nature, i.e., greater solubility in the aqueous system, not greater hydrophobic nature, i.e., less solubility in the aqueous system, to have been more effective. This point is quite clear, and Applicants fail to see any basis for the Examiner's contention that is not clear. The evidence in support of Applicants' arguments is in Applicants' examples. In contrast, the Examiner has cited no evidence whatsoever to support the contention that it would have been obvious to do what is claimed in claim 45. Accordingly, Applicants respectfully submit that there is no factual support for this rejection.

Accordingly, for this reason, in addition to the reasons above for the base claim, Applicants respectfully submit that the invention described in claim 45 would not have been obvious over the contended combination of Prusiner and Ernst and Race.

Applicants respectfully submit that claim 1 would not have been obvious over the prior art cited by the Examiner. Claims 31-55 depend from amended claim 1 and would not have been obvious over the cited references for at least the same reasons that claim 1 would not have been over such references. Withdrawal of the rejection is believed to be warranted and is respectfully requested.

Applicants respectfully submit that claim 56 would not have been obvious over the prior art cited by the Examiner. Claims 57-75 depend from claim 56 and also would not have been obvious over the cited references for the same reasons. Withdrawal of the rejection is believed to be warranted and is respectfully requested.

Conclusion

Applicants respectfully submit that the application is in condition for allowance. A Notice of Allowance is respectfully requested.

Any additional fees required for the filing of this paper may be charged to Deposit Account No. 18-0988. In the event the Examiner would like to discuss any matter involving this application with the Applicants, he is invited to contact the undersigned attorney by telephone.

Respectfully submitted,

RENNER, OTTO, BOISSELLE & SKLAR, LLP

By /thomaswadams/
Thomas W. Adams
Reg. No. 35,047

The Keith Building
1621 Euclid Avenue
Nineteenth Floor
Cleveland, Ohio 44115
216/621-1113